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A **polymorphism** in the **TCF7** locus is associated with type 1 diabetes in Caucasians.

AUTHOR: Noble J A(a); White A(a); Mirel D B; Valdes A M; Reynolds R; Zangenberg G; Lazzeroni L; Grupe A; Peltz G; Erlich H A(a)

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12621341 BIOSIS NO.: 200000374843

The human **T-cell transcription factor-4** gene:

Structure, extensive characterization of alternative splicings, and mutational analysis in colorectal cancer cell lines.

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ABSTRACT: The human **T cell transcription factor-4**

(hTCF-4) interacts functionally with beta-catenin in the Wnt signaling pathway, which regulates many developmental processes. Moreover, inappropriate reactivation of this pathway attributable to APC or beta-catenin mutations has been described in colorectal cancers. Because only the human TCF-4 cDNA sequence was known, we determined its genomic structure. A total of 17 exons, of which 5 were alternative, were identified. Moreover, four alternative splice sites were observed either experimentally or in silico by a BLAST approach in expressed sequence tag databases. The alternative use of three consecutive exons localized in the 3' part of the hTCF-4 gene changes the reading frames used in the last exon, leading to the synthesis of a number of hTCF-4 isoforms with short, medium, or long-size COOH-terminal ends. We next screened the entire hTCF-4 gene for mutations in a series of 24 colorectal cancer cell lines by denaturing gradient gel electrophoresis and/or direct sequencing. Besides an already described deletion of an A in an (A)9 coding repeat in four cases, we found DNA variants in eight cases for a total of 12 variants, of which 8 were coding. These include one frameshift **mutation** in the beta-catenin binding domain (exon 1), and one missense **mutation** in exon 4. In the remaining six cases, nonsense or frameshift mutations were localized in the 3' part of the gene. These latter alterations have as a common consequence to decrease the proportion of the long COOH-terminal hTCF-4 isoform, which contains two binding domains for c-terminal binding protein, a protein implicated in the repression of the TCF family transcriptional activity. Thus, loss of the TCF-4 capacity to interact with COOH-terminal binding protein

could be an important event during colorectal carcinogenesis by modifying Wnt signaling.

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DIALOG(R)File 73:EMBASE
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11151752 EMBASE No: 2001166276
LEF1 turns over a new leaf
De Lau W.; Clevers H.
W. De Lau, Department of Immunology, Center for Biomedical Genetics,
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Nature Genetics (NAT. GENET.) (United States) 2001, 28/1 (3-4)
CODEN: NGENE ISSN: 1061-4036
DOCUMENT TYPE: Journal ; Short Survey
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 15

LEF and TCF transcription factors (referred to collectively as LEF/TCFs) are pivotal players in the molecular pathology of cancer of the intestinal tract. Mutant components of the Wnt signal transduction cascade invariably lead to the inappropriate activation of LEF/TCFs in the cancer cell. A new study provides evidence for an unexpected amplification step in this cascade. The inappropriate activity of the Wnt pathway in colorectal cancer cells induces the expression of **LEF1**, which is normally not expressed in intestinal epithelium.

4/7/53 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
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136113776 CA: 136(8)113776c PATENT
TCF-1 gene polymorphic allele A (with mutation C883.fwdarw.A) associated with Th1 and Th2 diseases and therapeutic and diagnostic methods thereof
INVENTOR(AUTHOR): Begovich, Ann Bethea; Erlich, Henry Anthony; Gruppe, Andrew; Noble, Janelle Annette; Peltz, Gary Allen; Reynolds, Rebecca Lynne; Walker, Karen Myra; Zangenberg, Gabriele
LOCATION: Germany,
ASSIGNEE: Roche Diagnostics G.m.b.H.; F. Hoffmann-La Roche A.-G.
PATENT: European Pat. Appl. ; EP 1174522 A2 DATE: 20020123
APPLICATION: EP 2001116692 (20010717) *US PV219812 (20000721)
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DESIGNATED COUNTRIES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE; MC; PT; IE; SI; LT; LV; FI; RO
SECTION:
CA203001 Biochemical Genetics
CA206XXX General Biochemistry
CA213XXX Mammalian Biochemistry
CA214XXX Mammalian Pathological Biochemistry
IDENTIFIERS: TCF1 gene single nucleotide polymorphism genotyping, allele specific PCR primer TCF1 gene mutation detection, type I diabetes multiple sclerosis diagnosis therapy TCF1 polymorphism, allergic asthma atopy diagnosis therapy TCF1 polymorphism
DESCRIPTORS:
Alleles...
A or C, of TCF-1 gene; TCF-1 gene polymorphic allele A (with mutation C883.fwdarw.A) assocd. with Th1 and Th2 diseases and therapeutic and diagnostic methods thereof
Primers(nucleic acid)... Probes(nucleic acid)...
allele-specific; TCF-1 gene polymorphic allele A (with mutation C883.fwdarw.A) assocd. with Th1 and Th2 diseases and therapeutic and

diagnostic methods thereof

Asthma...
 allergic; TCF-1 gene polymorphic allele A (with mutation C883.fwdarw.A)
 assocd. with Th1 and Th2 diseases and therapeutic and diagnostic
 methods thereof

Allergy...
 atopy; TCF-1 gene polymorphic allele A (with mutation C883.fwdarw.A)
 assocd. with Th1 and Th2 diseases and therapeutic and diagnostic
 methods thereof

Population genetics...
 by analyzing Hardy-Weinberg disequil.; TCF-1 gene polymorphic allele A
 (with mutation C883.fwdarw.A) assocd. with Th1 and Th2 diseases and
 therapeutic and diagnostic methods thereof

Genetic element...
 exon, 2, of TCF-1 gene; TCF-1 gene polymorphic allele A (with mutation
 C883.fwdarw.A) assocd. with Th1 and Th2 diseases and therapeutic and
 diagnostic methods thereof

Transcription factors...
 gene TCF-1; TCF-1 gene polymorphic allele A (with mutation
 C883.fwdarw.A) assocd. with Th1 and Th2 diseases and therapeutic and
 diagnostic methods thereof

T cell(lymphocyte)...
 helper cell/inducer, TH1, diseases assocd. with; TCF-1 gene polymorphic
 allele A (with mutation C883.fwdarw.A) assocd. with Th1 and Th2
 diseases and therapeutic and diagnostic methods thereof

T cell(lymphocyte)...
 helper cell/inducer, TH2, diseases assocd. with; TCF-1 gene polymorphic
 allele A (with mutation C883.fwdarw.A) assocd. with Th1 and Th2
 diseases and therapeutic and diagnostic methods thereof

Gene, animal...
 HLA-DRB1, anal. of TCF-1 locus interaction with; TCF-1 gene polymorphic
 allele A (with mutation C883.fwdarw.A) assocd. with Th1 and Th2
 diseases and therapeutic and diagnostic methods thereof

Histocompatibility antigens...
 HLA-DR3, locus for, anal. of TCF-1 locus interaction with; TCF-1 gene
 polymorphic allele A (with mutation C883.fwdarw.A) assocd. with Th1 and
 Th2 diseases and therapeutic and diagnostic methods thereof

Histocompatibility antigens...
 HLA-DR4, locus for, anal. of TCF-1 locus interaction with; TCF-1 gene
 polymorphic allele A (with mutation C883.fwdarw.A) assocd. with Th1 and
 Th2 diseases and therapeutic and diagnostic methods thereof

Chromosome...
 human X, locus on, anal. of TCF-1 locus interaction with; TCF-1 gene
 polymorphic allele A (with mutation C883.fwdarw.A) assocd. with Th1 and
 Th2 diseases and therapeutic and diagnostic methods thereof

Oligonucleotides...
 immobilized; TCF-1 gene polymorphic allele A (with mutation
 C883.fwdarw.A) assocd. with Th1 and Th2 diseases and therapeutic and
 diagnostic methods thereof

Diabetes mellitus...
 insulin-dependent; TCF-1 gene polymorphic allele A (with mutation
 C883.fwdarw.A) assocd. with Th1 and Th2 diseases and therapeutic and
 diagnostic methods thereof

Diagnosis...
 mol.; TCF-1 gene polymorphic allele A (with mutation C883.fwdarw.A)
 assocd. with Th1 and Th2 diseases and therapeutic and diagnostic
 methods thereof

Mutation...
 point, C883.fwdarw.A in TCF-1 gene; TCF-1 gene polymorphic allele A
 (with mutation C883.fwdarw.A) assocd. with Th1 and Th2 diseases and
 therapeutic and diagnostic methods thereof

Genetic polymorphism...
 single nucleotide; TCF-1 gene polymorphic allele A (with mutation
 C883.fwdarw.A) assocd. with Th1 and Th2 diseases and therapeutic and

diagnostic methods thereof
Allele frequency... Disease, animal... DNA sequences... Drug screening...
Gene therapy... Genetic vectors... Genotyping(method)... Human... Molecular
cloning... Multiple sclerosis... Nucleic acid hybridization...
PCR(polymerase chain reaction)... Protein sequences...
TCF-1 gene polymorphic allele A (with mutation C883.fwdarw.A) assocd.
with Th1 and Th2 diseases and therapeutic and diagnostic methods
thereof
Gene, animal...
TCF-1; TCF-1 gene polymorphic allele A (with mutation C883.fwdarw.A)
assocd. with Th1 and Th2 diseases and therapeutic and diagnostic
methods thereof
CAS REGISTRY NUMBERS:
391286-09-2 391286-10-5 391286-11-6 391286-12-7 nucleotide sequence of
allele-specific primer; TCF-1 gene polymorphic allele A (with mutation
C883.fwdarw.A) assocd. with Th1 and Th2 diseases and therapeutic and
diagnostic methods thereof
141008-03-9 391286-13-8 nucleotide sequence; TCF-1 gene polymorphic
allele A (with mutation C883.fwdarw.A) assocd. with Th1 and Th2
diseases and therapeutic and diagnostic methods thereof
391292-10-7 391292-11-8 391292-12-9 391292-13-0 unclaimed nucleotide
sequence; tCF-1 gene polymorphic allele A (with mutation C883.fwdarw.A)
assocd. with Th1 and Th2 diseases and therapeutic and diagnostic
methods thereof
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